

Response to Restriction Requirement
And Second Preliminary Amendment

2968-B

SECOND PRELIMINARY AMENDMENTIN THE CLAIMS:

All of the pending claims are reiterated below. Claims not amended are marked "Reiterated".

Please cancel claims 4-5, 24-38, and 40-45, without prejudice.

Please amend claims 1, 6, 8, 13, and 16 as follows:

B1
1. (Amended) A method of modulating angiogenesis in a mammal in need of such treatment comprising administering a therapeutically-effective amount of a composition comprising an antagonist of a TWEAK receptor, wherein the TWEAK receptor comprises a sequence as set forth from amino acids 28-79 of SEQ ID NO:7 or naturally occurring variants thereof.

2. (Reiterated) The method of claim 1 wherein the composition further comprises a pharmaceutically acceptable carrier.

3. (Reiterated) The method of claim 2 wherein the mammal is a human.

B2
6. (Amended) The method of claim 1, wherein the antagonist is selected from the group consisting of a soluble TWEAK receptor fragment, an antibody, an antisense nucleic acid, a triple helix forming nucleic acid, a peptide, and a small molecule.

7. (Reiterated) The method of claim 6 wherein the antagonist comprises a soluble TWEAK receptor fragment.

B3
8. (Twice Amended) The method of claim 7, wherein the antagonist comprises:

- (a) an Fc polypeptide, leucine zipper domain, and/or peptide linker; and
- (b) about two to four polypeptides comprising a TWEAK receptor extracellular domain or fragments or variants thereof that are capable of binding TWEAK.

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9. (Reiterated) The method of claim 8 wherein the antagonist comprises an Fc polypeptide fused to: (a) a TWEAK receptor extracellular domain; or (b) a fragment or variant of (a) that is capable of binding TWEAK.

10. (Reiterated) The method of claim 9 wherein the TWEAK receptor extracellular domain comprises amino acids 28-79 of SEQ ID NO:7.

11. (Reiterated) The method of claim 10 wherein the antagonist comprises amino acids 28-309 of SEQ ID NO:7.

12. (Reiterated) The method claim 6 wherein the antagonist comprises an antibody that binds specifically to the TWEAK receptor extracellular domain.

B4 13. (Amended) The method of claim 12, wherein the antibody is selected from the group consisting of a monoclonal antibody, a humanized antibody, a transgenic antibody, and a human antibody.

14. (Reiterated) The method of claim 12 wherein the antibody is conjugated to a radioisotope, to a plant-, fungus-, or bacterial-derived toxin such as ricin A or diphtheria toxin, or to another chemical poison.

15. (Reiterated) The method of claim 6 wherein the antagonist disrupts the interaction between the TWEAK receptor and a TRAF molecule.

B5 16. (Amended) The method of claim 2, wherein the mammal has a disease or condition mediated by angiogenesis.

17. (Reiterated) The method of claim 16 wherein the disease or condition is characterized by ocular neovascularization.

18. (Reiterated) The method of claim 16 wherein the disease or condition is a solid tumor.

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19. (Reiterated) The method of claim 16 wherein the method further comprises treating the mammal with radiation.
20. (Reiterated) The method of claim 16 wherein the method further comprises treating the mammal with a second chemotherapeutic agent.
21. (Reiterated) The method of claim 20 wherein the second chemotherapeutic agent is selected from the group consisting of alkylating agents, antimetabolites, vinca alkaloids and other plant-derived chemotherapeutics, nitrosoureas, antitumor antibiotics, antitumor enzymes, topoisomerase inhibitors, platinum analogs, adrenocortical suppressants, hormones, hormone agonists, hormone antagonists, antibodies, immunotherapeutics, blood cell factors, radiotherapeutics, and biological response modifiers.
22. (Reiterated) The method of claim 20 wherein the second chemotherapeutic agent is selected from the group consisting of cisplatin, cyclophosphamide, mechlorethamine, melphalan, bleomycin, carboplatin, fluorouracil, 5-fluorodeoxyuridine, methotrexate, taxol, asparaginase, vincristine, and vinblastine, lymphokines and cytokines such as interleukins, interferons (including alpha, beta, or delta), and TNF, chlorambucil, busulfan, carmustine, lomustine, semustine, streptozocin, dacarbazine, cytarabine, mercaptopurine, thioguanine, vindesine, etoposide, teniposide, dactinomycin, daunorubicin, doxorubicin, bleomycin, plicamycin, mitomycin, L-asparaginase, hydroxyurea, methylhydrazine, mitotane, tamoxifen, and fluoxymesterone.
23. (Reiterated) The method of claim 20 wherein the second chemotherapeutic agent is selected from the group consisting of Flt3 ligand, CD40 ligand, interleukin-2, interleukin-12, 4-1BB ligand, anti-4-1BB antibodies, TNF antagonists and TNF receptor antagonists, TRAIL, CD148 agonists, VEGF antagonists, VEGF receptor antagonists, and Tek antagonists.

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